REMARKS

Claims 1-2 and 7-38 are presently pending. Claims 3-6 have been canceled without prejudice. Claims 1, 2, 7-10 and 12 have been amended to more particularly point out and distinctly claim the subject matter. No new matter has been added.

I. Restriction of Claims 12-37

Claims 12-37 have been withdrawn from consideration (Office Action, page 9, lines 14-15) under MPEP §806.05(h) unless Applicants elect a specific disease.

With respect to claims 24-37, Applicants elect an inflammatory condition (claims 24-27) without in any way conceding the merits of the Examiner's restriction requirement and solely to advance the prosecution of this application. With respect to claim 12, however, Applicants respectfully decline to elect a specific disease because this claim relates to a method for treating *any* condition responsive to IKK-2 inhibition. In particular, claim 12 relates to the ability of the anilinopyrimidine derivatives of formula (I) (page 5, line 23 to page 6, line 27) to inhibit IKK-2 and their resultant usefulness for treating a condition responsive to IKK-2 inhibition, such an inflammatory or autoimmune condition, a cardiovascular condition, a metabolic or ischemic condition, an infectious disease or cancer. Accordingly, Applicants do not wish to limit claim 12 to a particular condition.

In view of Applicants' election of claims 24-27, Applicants believe that a prior art search in connection with claim 12, however, would impose no undue burden on the Examiner because an inflammatory condition *is an example of a condition responsive to IKK-2 inhibition* (page 19, lines 4-9). Accordingly, Applicants respectfully traverse the restriction requirement with respect to claim 12 and request that the Examiner also examine this claim in the present application.

Should the Examiner agree to examine claim 12 in the present application, then Applicants respectfully request that claims 13 and 14, in which the condition responsive to IKK-2 inhibition is an inflammatory or autoimmune condition, also be examined. Should the Examiner limit Applicants' election to claims 24-27, however, then Applicants wish to have the subject matter of claims 12-14 examined together in a subsequently filed continuation, continuation-in-part or divisional application.

The Examiner has also indicated that claims 23, 25, 26, 27, 34 and 35 must be restricted out (Office Action, page 10, last three lines) for allegedly not being of the same scope because they comprise additional active ingredients. The Examiner alleges that the

additional search would be burdensome. Applicants respectfully traverse the restriction. Applicants respectfully submit that no additional search would be required, as each of claims 25, 26 and 27 (claims 23, 34 and 35 having not been elected) is dependent from elected claim 24; thus, any search of method claim 24 should uncover any reference that might disclose the use of additional agents.

Accordingly, Applicants respectfully request that claims 25-27 be examined with claim 24 in the present application.

II. The Rejection Under 35 U.S.C. §112, First Paragraph

Claims 1, 2, 4, 6, 7 and 12 have been rejected under 35 U.S.C. §112, first paragraph (Office Action, page 3, line 1; page 9, lines 6 and 10), as allegedly not containing adequate representative exemplification for the breadth of the claims with respect to the term "heteroaryl."

The specification at page 9, lines 12-15 clearly defines what is meant by "heteroaryl" and gives numerous examples of representative heteroaryl groups (*e.g.*, pyridyl, furyl, benzofuranyl, thiophenyl, benzothiophenyl, quinolinyl, pyrrolyl, indolyl, oxazolyl, benzoxazolyl, imidazolyl, benzimidazolyl, thiazolyl, benzothiazolyl, isoxazolyl, pyrazolyl, isothiazolyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, cinnolinyl, phthalazinyl, and quinazolinyl). However, without in any way conceding the merits of this rejection and solely to advance the prosecution of this application, Applicants have amended claims 1 and 12 to delete the term "heteroaryl" and to recite the specific "heteroaryl" groups disclosed in the specification at page 9, lines 9-15. Claims 2 and 7 do not recite the term "heteroaryl" and claims 4 and 6 have been canceled without prejudice.

Accordingly, Applicants believe that the rejection of claims 1, 2, 4, 6, 7 and 12 under 35 U.S.C. §112, first paragraph, as allegedly not containing adequate representative exemplification for the breadth of the claim cannot stand and must be withdrawn.

III. The Rejection Under 35 U.S.C. §112, Second Paragraph

Claims 1, 2, 4, 6, 7 and 12 have been rejected under 35 U.S.C. §112, second paragraph (Office Action, page 2, lines 1 and 11; page 9, lines 6 and 10), as allegedly indefinite due to the recitation of the terms "aryl", "heteroaryl" and "heterocycle." The Examiner has suggested that a Markush listing of intended, conceived of, producible, heterocyclic rings is needed (Office Action, page 6, lines 6-8).

MPEP §608.01(o) states that the meaning of every term used in any of the claims should be apparent from the descriptive portion of the specification. The meaning of the terms "aryl", "heterocycle" and "heteroaryl" is readily apparent from the descriptive portion of the specification. The specification clearly defines: "aryl" (page 9, line 5) as an aromatic carbocyclic moiety and sets forth phenyl or naphthyl as representative aryls; "heterocycle" (page 9, lines 19-30) as a 5- to 7-membered monocyclic, or 7- to 10-membered bicyclic, heterocyclic ring which is either saturated, unsaturated, or aromatic, and which contains from 1 to 4 heteroatoms independently selected from nitrogen, oxygen and sulfur, and sets forth numerous representative examples of "heterocycles"; and "heteroaryl" (page 9, lines 9-15) as an aromatic heterocycle ring of 5- to 10 members and having at least one heteroatom selected from nitrogen, oxygen and sulfur, and containing at least one carbon atom, including both mono- and bicyclic ring systems, and discloses numerous representative "heteroaryl" groups.

These sections of the specification clearly answer the Examiner's questions as to the heteroaryl ring heteroatoms, the number of heteroatoms present in the ring(s) (Office Action, page 2, lines 12-13) and the size of the ring(s) (Office Action, page 5, line 6). These sections also clearly state that the heteroaryl group's heteroatom is selected from nitrogen, oxygen or sulfur (page 5, lines 10-11 of the specification), which does not include B, P or As as suggested by the Examiner (Office Action, page 5, line 11).

However, without in any way conceding the merits of this rejection and solely to advance the prosecution of this application, Applicants have amended the claims to delete the recitation of the terms "aryl" (claims 1, 7 and 12), "heterocycle" (claims 1, 2, 8-10 and 12) and "heteroaryl" (claims 1 and 12) and to recite the specific "aryl", "heterocycle" and "heteroaryl" groups disclosed in the specification at page 5, line 9 (aryl); and page 9, lines 9-15 (heteroaryl) and lines 19-30 (heterocycle). Claims 4 and 6 have been canceled without prejudice.

Accordingly, Applicants believe that the rejection of claims 1, 2, 4, 6, 7 and 12 under 35 U.S.C. §112, second paragraph, as allegedly indefinite due to the recitation of the terms "aryl", "heterocycle" and "heteroaryl" cannot stand and must be withdrawn.

IV. The Rejection Under 35 U.S.C. §103(a)

Claims 4 and 6 have been rejected under 35 U.S.C. §103(a) (Office Action, page 7, lines 15 and 16; page 9, lines 1-5) as allegedly obvious over imidazo[1,2a]pyrid-3-yl

substituted or pyrazolo[2,3]pyrid-3-yl substituted compounds removed by proviso. Applicants have canceled claims 4 and 6 without prejudice, rendering the rejection moot.

Accordingly, Applicants request that the rejection under 35 U.S.C. §103(a) be withdrawn.

V. The Rejction Under 35 U.S.C. §§101 and 112, First Paragraph

Claim 12 has been rejected under 35 U.S.C. §§101 and 112, first paragraph, as allegedly lacking utility. The Examiner has alleged that the method of claim 12 does not meet the real World of Commerce requirement (Office Action, p. 10, line 11). Applicants respectfully traverse.

The PTO cannot reject a claim under 35 U.S.C. §112, first paragraph, for failure to teach how to use the invention and under 35 U.S.C. §101 for lack of utility unless it has reason to doubt the objective truth of the statements contained in the written description. And only after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence sufficient to convince such a person of the invention's asserted utility. *In re Cotright*, 165 F.3d 1353, 1357, 49 U.S.P.Q.2d 1464, 1466 (Fed. Cir. 1999).

As set forth in the Specification at page 1, line 13 to page 4, line 11, it is well known in the art that IKK-2 inhibitors are useful for treating numerous diseases, particularly inflammation. IKK-2 is a key regulatory signaling molecule that coordinates the activation of NF-κB. NF-κB is a key regulator of inflammatory gene transcription and is activated in the rheumatoid arthritis synovium (Aupperle et al. *J. Immunol. 163*:427-433,1999). The expression of more than 70 known proteins is transcriptionally regulated by the binding of NF-κB to specific sequence elements in the promoter region of these genes (Baeuerle and Baichwal, *Advances in Immunology 65*:111 -137, 1997). Because of its role in regulating NF-κB, IKK-2 has also been implicated in many pathophysiologic processes including angiogenesis (Koch et al., *Nature 376*:517-519, 1995), atherosclerosis (Brand et al., *J Clin Inv. 97*:1715-1722, 1996), endotoxic shock and sepsis (Bohrer et al., *J. Clin. Inv.* 100:972-985, 1997), inflammatory bowel disease (Panes et al., *Am J Physiol. 269*:H1955-H1964, 1995), ischemia/reperfusion injury (Zwacka et al., *Nature Medicine 4*:698-704, 1998), and allergic lung inflammation (Gosset et al., *Int Arch Allergy Immunol. 106*:69-77, 1995). Thus, because of the significant role of IKK-2 in numerous diseases, inhibition of IKK-2 is an art-accepted strategy for treating or preventing diseases, including, but not limited to,

angiogenesis, atherosclerosis, endotoxic shock, sepsis, inflammatory bowel disease, ischemia/reperfusion injury, allergic lung inflammation and, particularly, inflammation.

In view of the abundance of evidence provided showing the art's recognition of the usefulness of IKK-2 inhibitors for treating disease, Applicants respectfully submit that the PTO has a particularly high burden of showing that one of ordinary skill in the art would reasonably doubt the usefulness of the present anilinopyrimidine derivatives for treating a condition responsive to IKK-2 inhibition. Until the PTO has met its burden, however, Applicants believe that the rejection of claim 12 under 35 U.S.C. §§101 and 112, first paragraph, cannot stand and must be withdrawn.

VI. The Rejection of Claims 3, 5, 8-11 and 38 for Depending From a Rejected Claim

Claims 3, 5, 8-11 and 38 have been rejected for depending on a rejected claim (Office Action, page 9, lines 8-9) and not for reasons within themselves. In view of the above discussion, Applicants believe that the claims from which claims 3, 5, 8-11 and 38 depend are allowable. Accordingly, Applicants believe that claims 3, 5, 8-11 and 38 are allowable and respectfully request that the rejection of claims 3, 5, 8-11 and 38 be withdrawn.

VII. References AA-DF Cited in Information Disclosure Statement Filed August 28, 2002

Applicants have noticed that the Office Action does not include an Examiner-initialed version of a revised PTO form 1449 listing References AA-DF, which was filed with an Information Disclosure Statement and a copy of the References on August 28, 2002 in connection with the present application (Applicants enclose a copy of a return-receipt postcard (both sides) that the PTO stamped "AUG 28 2002," indicating its receipt of these items on that date). Accordingly, Applicants respectfully request that the Examiner make References AA-DF of record by reviewing the References and initializing the revised PTO form 1449 (an additional copy being enclosed for the Examiner's convenience).

VIII. Conclusion

Applicants respectfully request that the present remarks be made of record in the file history of the present application. An early allowance of the application is earnestly requested. The Examiner is invited to call the undersigned with any questions concerning the foregoing.

It is believed that no fee is due other than that for the extension of time; however, in the event any other fee is required, please charge the required fee to Pennie & Edmonds LLP Deposit Account No. 16-1150.

Respectfully submitted,

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Date May 27, 2003 By: Marcelo E. Lauper, Reg. No. 36,343

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Enclosures